

What Is Claimed Is:

1. A method of raising a broadly neutralizing antibody response to HIV, comprising:

5 administering to a mammal a peptide or polypeptide comprising an amino acid that is capable of forming a stable coiled-coil solution structure corresponding to or mimicking the heptad repeat region of gp41, or a fragment thereof.

2. The method of claim 1, wherein a peptide is administered, and wherein said peptide comprises about 28 to 55 amino acids of the following sequence:

ARQLLSGIVQQQNLLRAIEAQHQHLLQLTVWGIKQLQARILAVERYLKDQQLLG
10 (SEQ. ID NO:1), or multimers thereof.

3. The method of claim 2, wherein the peptide is conjugated to a carrier protein.

4. The method of claim 3, wherein said carrier protein is keyhole limpet hemocyanin (KLH), ovalbumin, bovine serum albumin (BSA) or tetanus toxoid.

15 5. The method of claim 1, wherein said peptide is one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, or one of SEQ ID NO: 9 through SEQ ID NO: 40; and wherein the peptide can be optionally coupled to a larger carrier protein, or optionally include a terminal protecting group at the N- and/or C- termini.

20 6. The method of claim 1, wherein said peptide has the formula, from amino terminus to carboxy terminus, of:

NH₂-NNLLRAIEAQHQHLLQLTVWGIKQLQARILAVERYLKDQ-COOH
(SEQ ID NO:1);

or:

NH₂-SGIVQQQNLLRAIEAQHQHLLQLTVWGIKQLQARIL-COOH

25 (SEQ ID NO:2);

and wherein the peptide can be optionally coupled to a larger carrier protein, or optionally include a terminal protecting group at the N- and/or C- termini.

7. The method of claim 1, wherein said peptide includes one to 10 conservative substitutions.

5 8. A method of raising a broadly neutralizing antibody response to HIV, comprising:

10 administering to a mammal a peptide or polypeptide comprising an amino acid sequence that corresponds to, or mimics, the transmembrane-proximal amphipathic α -helical segment of gp41 (at the C-helical domain of gp41), or a fragment thereof, wherein said mammal raises antibodies to a helical solution structure of said peptide or polypeptide.

9. The method of claim 8, wherein a peptide is administered, and wherein said peptide comprises about 24-56 amino acids of the following sequence:

15 WNNMTWMEWDREINNYTSЛИHSLIEESQNQQEKNEQELLELDKWASLWNWF
NITNW (SEQ ID NO:4), or a multimer thereof.

10. The method of claim 8, wherein the peptide or polypeptide is conjugated to a carrier protein.

11. The method of claim 10, wherein said carrier protein is keyhole limpet hemocyanin (KLH), ovalbumin, bovine serum albumin (BSA) or tetanus toxoid.

20 12. The method of claim 8, wherein said peptide includes one to 10 conservative substitutions.

13. The method of claim 8, wherein said peptide one of SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, or one of SEQ ID NO: 41 through SEQ ID NO: 74;

and wherein the peptide can be optionally coupled to a larger carrier protein, or optionally include a terminal protecting group at the N- and/or C- termini.

14. The method of claim 8, wherein said peptide has the formula, from amino terminus to carboxy terminus, of:

5 NH₂-YTSЛИHSLIЕEESQNQQEKNEQELLELDKWASLWNWF-COOH

(SEQ ID NO:3);

or:

NH₂-WMEWDREINNYTSЛИHSLIЕEESQNQQEKNEQELL-COOH

(SEQ ID NO:4)

10 and wherein the peptide can be optionally coupled to a larger carrier protein, or optionally include a terminal protecting group at the N- and/or C- termini.

15. A method of raising a broadly neutralizing antibody response to HIV, comprising:

15 administering to a mammal a composition including one or more peptides or polypeptides which comprise amino acid sequences that are capable of forming solution stable structures that correspond to, or mimic, the gp41 core six helix bundle.

16. The method of claim 15, wherein said one or more peptides or polypeptides comprise a mixture of C-helical peptide or polypeptide and N-helical peptide or polypeptide.

20 17. The method of claim 15, wherein at least one of said peptides or polypeptides is multimeric, or is a conjugate structure comprised of an N-helical domain amino acid sequence and a C-helical domain amino acid sequence.

25 18. The method of claim 15, wherein said mixture of C-helical peptide or polypeptide and N-helical peptide or polypeptide forms a stable core helix solution structure.

19. The method of claim 15, wherein said mixture comprises:

P-17 and P-18,

P-15 and P-16,

P-17 and P-16 or

5 P-15 and P-18.

20. A method of raising a broadly neutralizing antibody response to HIV, comprising:

administering to a mammal a composition including one or more conjugate peptides or polypeptides formed from two or more amino acid sequences that comprise:

10 (a) one or more amino acid sequences that are capable of forming a stable coiled-coil solution structure corresponding to or mimicking the heptad repeat region of gp41 (N-helical domain); and

(b) one or more amino acid sequences that correspond to, or mimic, an amino acid sequence of the transmembrane-proximal amphipathic α -helical segment of gp41
15 (C-helical domain);

wherein

said one or more sequences (a) and (b) are alternately linked to one another via a bond, such as a peptide bond (amide linkage) or by an amino acid linking sequence consisting of about 2 to about 25 amino acids.

20 21. The method of claim 20, wherein said conjugates are recombinantly produced.

22. The method of claim 21, wherein one or more of said conjugates folds and assembles in solution into a structure corresponding to, or mimicking, the gp41 core six helix bundle.

25 23. The method of claim 20, wherein:
said N-helical peptide comprises about 28 to 55 amino acids of the following sequence:

ARQLLSGIVQQQNNLLRAIEAQHQHLLQLTVWGIKQLQARILAVERYLKDDQQLLG
(SEQ. ID NO:1), or multimers thereof; and

said C-helical peptide comprises about 24-56 amino acids of the following sequence:

5 WNNMTWMEWDREINNYTSIHSILIEESQNQKEKNEQELLELDKWASLWNWF
NITNW (SEQ ID NO:4), or multimers thereof.

24. The method of claim 14 or claim 20, wherein:

said N-helical peptide is one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, or one of SEQ ID NO: 9 through SEQ ID NO: 40, and wherein the peptide can be 10 optionally coupled to a larger carrier protein, or optionally include a terminal protecting group at the N- and/or C- termini; and

said C-helical peptide is one of SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, or one of SEQ ID NO: 41 through SEQ ID NO: 74, and wherein the peptide can be 15 optionally coupled to a larger carrier protein, or optionally include a terminal protecting group at the N- and/or C- termini.

25. A conjugate peptide or polypeptide formed from two or more amino acid sequences that comprise:

- (a) one or more amino acid sequences that are capable of forming a stable coiled-coil solution structure corresponding to or mimicking the heptad repeat region of gp41 (N-helical domain); and
- (b) one or more amino acid sequences that correspond to, or mimic, an amino acid sequence of the transmembrane-proximal amphipathic α -helical segment of gp41 (C-helical domain);

wherein

25 said one or more sequences (a) and (b) are alternately linked to one another via a bond, such as a peptide bond (amide linkage) or by an amino acid linking sequence consisting of about 2 to about 25 amino acids.

26. The conjugate of claim 25, wherein:

said N-helical peptide comprises about 28 to 55 amino acids of the following sequence:

ARQLLSGIVQQQNLLRAIEAQQHLLQLTVWGIKQLQARILAVERYLKDQQLLG

5 (SEQ. ID NO:1), or multimers thereof; and

said C-helical peptide comprises about 24-56 amino acids of the following sequence:

WNNMTWMEWDREINNYTSLIHSLIESQNQQEKNEQELLELDKWASLWNWF
NITNW (SEQ ID NO:4), or multimers thereof.

10 27. The conjugate of claim 25, wherein:

said N-helical peptide is one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, or one of SEQ ID NO: 9 through SEQ ID NO: 40, and wherein the peptide can be optionally coupled to a larger carrier protein, or optionally include a terminal protecting group at the N- and/or C- termini; and

15 said C-helical peptide is one of SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, or one of SEQ ID NO: 41 through SEQ ID NO: 74, and wherein the peptide can be optionally coupled to a larger carrier protein, or optionally include a terminal protecting group at the N- and/or C- termini.

20 28. A pharmaceutical composition comprising a conjugate of claim 25, and a pharmaceutical acceptable carrier.

29. A composition comprising polyclonal or monoclonal antibodies that are raised to the conjugate of claim 25.

25 30. A composition comprising a mixture of C-helical peptide or polypeptide and N-helical peptide or polypeptide, wherein said mixture forms a stable core helix solution structure.

31. The composition of claim 30, wherein:

said N-helical peptide comprises about 28 to 55 amino acids of the following sequence:

ARQLLSGIVQQQNLLRAIEAQHQHLLQLTVWGIKQLQARILAVERYLKDQQQLGI

5 (SEQ. ID NO:1), or multimers thereof; and

said C-helical peptide comprises about 24-56 amino acids of the following sequence:

WNNMTWMEWDREINNYTSЛИHSLIEESQNQQEKNEQELLELDKWASLWNWF
NITNW (SEQ ID NO:4), or multimers thereof.

10 32. The composition of claim 30, wherein:

said N-helical peptide is one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, or one of SEQ ID NO: 9 through SEQ ID NO: 40, and wherein the peptide can be optionally coupled to a larger carrier protein, or optionally include a terminal protecting group at the N- and/or C- termini; and

15 said C-helical peptide is one of SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, or one of SEQ ID NO: 41 through SEQ ID NO: 74, and wherein the peptide can be optionally coupled to a larger carrier protein, or optionally include a terminal protecting group at the N- and/or C- termini.

20 33. A composition comprising polyclonal or monoclonal antibodies that are raised to the composition of claim 30.

34. A method of treatment, comprising:

25 administering to an individual a composition comprising polyclonal or monoclonal antibodies as claimed in claim 29 or claim 33 in an amount effective to reduce HIV infection of uninfected cells.

35. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence encoding a peptide or polypeptide conjugate of claim 25.

36. The nucleic acid molecule of claim 35, wherein said polynucleotide has the nucleotide sequence in FIG. 7.

37. A method for making a recombinant vector comprising inserting an isolated nucleic acid molecule of claim 35 into a vector.

5 38. A recombinant vector produced by the method of claim 37.

39. A method of making a recombinant host cell comprising introducing the recombinant vector of claim 38 into a host cell.

40. A recombinant host cell produced by the method of claim 39.

10 41. A recombinant method for producing a conjugate peptide or polypeptide, comprising culturing the recombinant host cell of claim 40 under conditions such that said polypeptide is expressed and recovering said polypeptide.

42. The method of claim 1, claim 8, claim 15 or claim 20, wherein said administering is provided in advance of any symptoms of HIV infection, or in advance of any known exposure to HIV.

15 43. The method of claim 1, claim 8, claim 15 or claim 20, wherein said administering is provided upon or after the detection of symptoms which indicate that an animal may be infected with HIV, or upon or after exposure to the virus.